1.a. Full Title: Ambient air pollution is associated with the onset of acute events – The ARIC Study

b. Abbreviated Title (Length 26 characters): Pollution, MI, stroke, and SCD

2. Writing Group:

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I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. {Duanping Liao}

3. Timeline:

Initial analyses and writing will take place between March and August 2006, and final writing and manuscript submission between August and December 2006.

4. Rationale:

Considerable numbers of epidemiological studies have linked short-term changes in the concentrations of ambient air pollutants, especially fine particles, with changes in daily morbidity, mortality, and hospitalization from cardiopulmonary diseases (1-12). The underlying biological mechanisms linking ambient air pollution and cardiopulmonary disease continue to be a subject of research. Several hypotheses have been proposed, including the adverse effects of air pollutants on cardiac autonomic control, systemic inflammation, and enhanced blood coagulation (13-20). Most of these studies have
suggested acute adverse effects of air pollution on cardiovascular health. Recently, several case-crossover studies have reported the acute adverse effects of air pollution, especially particulate matter (PM) pollution, on myocardial infarction and stroke\(^{(21-26)}\). However, several studies have also reported a lack of association between air pollution and stroke admission or myocardial infarction\(^{(27-30)}\). To our knowledge, no one has published associations between particle components and the risk of incident events.

We propose to investigate the short-term, acute effects of ambient pollutants (PM\(_{10}\), O\(_3\), NO\(_2\), and SO\(_2\)) on the onset of incident myocardial infarction, ischemic stroke, and sudden death in the ARIC cohort, using a case-crossover approach. Our operational hypothesis is that higher ambient levels of pollutants, especially PM, trigger the onset of myocardial infarction, ischemic stroke, and sudden death.

We will select all incident cases of MI (excluding ECG MI), ischemic stroke, and sudden death, using the official events variables. These cases will form our study population. Case periods will be defined as zero to two days prior to the date of onset (i.e. lag2, where lag0 = date of onset). Control periods will be defined as about 7-9 days prior to the date of onset of an event (lag7-lag9), matching on the day of the week to eliminate the bias. That is, if exposure of interest is lag 0 (date of onset), control period would be lag 7; if exposure of interest is 1 day prior to onset (lag 1), the control period will be lag 8; and if exposure interest is the average of lag 0 - 2 (three day average), the control period will be lag 7-9 (three day average). This way, the exposure period and control period will always be identical in terms of day of the week. Participants’ exposures during case and control periods will be calculated from ambient air pollution concentration data that we have obtained and used in our ARIC ancillary study (AS# 1998.01). They will be supplemented with recently available particle components data from the EPA Air Quality System. Specifically, air pollution exposures will be calculated as 24-hour average pollutant concentrations at each ARIC study field center as previously reported\(^{(15, 18, 31)}\). Conditional logistic regression will be used to estimate associations (odds ratios, 95% CIs) between case-control status and air pollution concentrations measured during the
case and control periods. Sensitivity of estimates to alternative control period definitions will be examined (32).

5. Main Hypothesis/Study Questions:

1. Are CVD events associated with short-term exposures to air pollutants and particle components?
2. If so, are the associations modified by the conventional CVD risk factor profile (smokers, older age, prevalent diabetes, and prevalent hypertension)?

6. Data (variables, time window, source, inclusions/exclusions):

(1) Air pollution variables – from our ARIC ancillary study and supplemented as described above.
(2) Incident CVD events: from official events databases, including incident MI, ischemic stroke, and sudden death.
(3) Covariates: age, sex, ethnicity, center, smoking, diabetes, hypertension, and other conventional CVD risk factors.
(4) Exclusion criteria: Prevalent CHD or prevalent stroke at the baseline examination.

7.a. Will the data be used for non-CVD analysis in this manuscript? ____ Yes  _X_ No

b. If Yes, is the author aware that the file ICTDER01 must be used to exclude persons with a value RES_OTH = “CVD Research” for non-DNA analysis, and for DNA analysis RES_DNA = “CVD Research” would be used? ____ Yes  ____ No
(This file ICTDER01 has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8.a. Will the DNA data be used in this manuscript?  ____ Yes  _X_ No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER01 must be used to exclude those with value RES_DNA = “No use/storage DNA”? ____ Yes  ____ No

9. The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status. ARIC Investigators have access to the publications lists under the
10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)?


11. a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data?  

   _X_ Yes  

   ____ No

11.b. If yes, is the proposal  

   _X_ A. primarily the result of an ancillary study (list number* _1998.01_)  

   ____ B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* __________   __________ ___________

*ancillary studies are listed by number at [http://www.cscc.unc.edu/aric/forms/](*.

12. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire.

References


18. Duanping Liao, Gerardo Heiss, Vernon M. Chinchilli, Yinkang Duan, Aaron R. Folsom, Hung-Mo Lin, Veikko Salomaa: Association of criteria pollutants with plasma


